

Acute pericarditis, Graves' disease, and thymic hyperplasia: a case report

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Background

Acute pericarditis as a sign of mediastinal mass is rare and aetiological diagnosis can be challenging without adequate imaging.

Case summary

An 18-year-old woman came to our attention describing acute sharp chest pain radiated to the left arm, exacerbated with supine positioning and attenuated while sitting or leaning forward. The electrocardiogram showed diffuse ST elevation and PR depression, with sinus tachycardia. Cardiac biomarkers and D-dimer were negative; echocardiography showed no abnormalities and the absence of pericardial effusion. Her blood work revealed no sign of inflammation or bacterial infection (PCR and procalcitonin were normal); thyroid-stimulating hormone plasma levels were suppressed, showing decompensated thyrotoxicosis. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), Epstein–Barr virus, human immunodeficiency virus, hepatitis C virus, Enterovirus, Parvovirus B19, and Adenovirus tests were normal. Her past medical history was silent, apart from Graves' disease on treatment with methimazole. Chest computed tomography (CT) was performed and showed the presence of slightly increased density pericardial effusion, with a maximum thickness of 15 mm in the upper mediastinum. Finally, cardiac magnetic resonance (MR) identified a mass of 73 × 51 mm located in the upper mediastinum. The mass was subsequently biopsied with video-assisted thoracoscopic surgery and the histological analysis showed thymic hyperplasia.

Discussion

This case shows the importance of an adequate clinical suspicion of thymic hyperplasia in the context of acute pericarditis symptoms and known Graves' disease. In this case, a negative chest CT finding may not be sufficient to rule out the diagnosis and cardiac MR imaging is necessary.

Keywords

Graves' • disease • Acute pericarditis • Thymic hyperplasia • Cardiac MR • Case report

Learning points

- Graves' disease and uncontrolled hyperthyroidism can induce thymic hyperplasia.
- Acute pericarditis may be the first clinical presentation of thymic hyperplasia.
- In this case, a negative chest computed tomography finding may not be sufficient to rule out the diagnosis and cardiac magnetic resonance imaging is necessary.

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Introduction

According to the European Society of Cardiology (ESC) guidelines on pericardial diseases, the clinical diagnosis of acute pericarditis can be made with at least two criteria out of four: (i) chest pain improved by leaning the chest forward and in a sitting position; (ii) friction rub; (iii) electrocardiogram (ECG) changes such as widespread ST elevation or PR depression; and (iv) pericardial effusion.¹ From the aetiological point of view, mediastinal mass can be a cause of pericarditis, both by direct effect, often inducing chronic constrictive forms, and by paraneoplastic and drug (chemotherapy-induced) effects.² Thymic hyperplasia may represent a cause of chest pain in the young, however, to date only one case of acute pericarditis secondary to thymic hyperplasia and hyperthyroidism has been described.³ In this clinical setting, chest computed tomography (CT) may not be sufficient for ruling out the diagnosis of thymic hyperplasia-related pericarditis.

Timeline

Time	Event
10 October	Acute pericarditis symptoms onset in the morning.
10 October 12:15	Access to the emergency department for persisting symptoms.
10 October 12:30	The electrocardiogram (ECG) showed tachycardia at 128 b.p.m. and diffuse, concave ('saddle-shaped') and non-specific ST-segment elevations in all leads except aVR and V1, and PR-segment depression except aVR.
10 October 13:30	Laboratory findings show no significant abnormalities. In particular, cardiac markers, D-dimer, complete blood count, C-reactive protein, and procalcitonin are normal.
10 October 17:00	Analgesic drugs are administered and the patient is hospitalized in the Cardiology Department.
10 October 17:30	Transthoracic echocardiography is performed, showing a normal left ventricular ejection fraction (EF = 65%), absence of valvular diseases, no pericardial effusion, and normal right ventricular dimensions and function.
11 October 01:00	Thoracic non-ECG-gated computed tomography (CT) angiography is performed and acute aortic and pulmonary diseases are ruled out. The CT shows the presence of a pericardial effusion with slightly increased density having a maximum

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Time	Event
	thickness of 15 mm in the upper mediastinum.
12 October 11:00	Further laboratory tests show no significant abnormalities except for thyroid-stimulating hormone (TSH) suppression (<0.0008 mIU/L) and increased serum-free thyroxine 4 (61.24 pg/mL); Epstein-Barr virus, human immunodeficiency virus, hepatitis C virus, Enterovirus, Parvovirus B19, and Adenovirus are negative. Antithyroid therapy is optimized and propranolol introduced.
12 October 17:00	Cardiac magnetic resonance imaging (MRI) is performed and the effusion turns out to be a mass of 73 × 51 mm located in the upper mediastinum.
15 October 11:00	Video-assisted thoracoscopic surgery and mass biopsy are performed, demonstrating thymic hyperplasia.
17 October 10:00	After symptoms improvement, the patient is discharged and ambulatory follow-up planned.
4 November 9:00	At the ambulatory follow-up visit, patient is asymptomatic, TSH level are normal and a 12-month cardiac MRI is planned.

Case presentation

We describe the case of an 18-year-old woman with chest pain radiating to the left arm at rest. Her past medical history was unremarkable, apart from Graves' disease on treatment with methimazole at a dosage of 5 mg/die. She came to our attention in 2020, when she was admitted to the emergency department (ED) for the onset of sharp chest pain radiated to the left arm and to the trapezius ridge. Pain was less severe when in a seated position and more severe when in a supine position, when breathing deeply or during coughing. No episodes of fever, diarrhoea, respiratory symptoms, or myalgia were reported in the previous days. In the ED, the pain was persistent; laboratory findings showed no significant abnormalities. In particular, cardiac markers, D-dimer, complete blood count, C-reactive protein, and procalcitonin were normal. The ECG (*Figure 1*) showed tachycardia at 128 b.p.m. and diffuse, concave ('saddle-shaped') and non-specific ST-segment elevations in all leads except aVR and V1, and PR-segment depression except aVR. Analgesic drugs were administered and the patient was then hospitalized in the Cardiology Department for further diagnostic and therapeutic assessment. On physical examination, blood pressure was 141/63 mmHg and body temperature 36.5°C. On cardiac auscultation, S1 and S2 heart sounds were normal and no pathological murmur was reported; no friction rub was heard. Absence of jugular vein distension and no pulsus paradoxus was reported. Laboratory tests were repeated and showed no

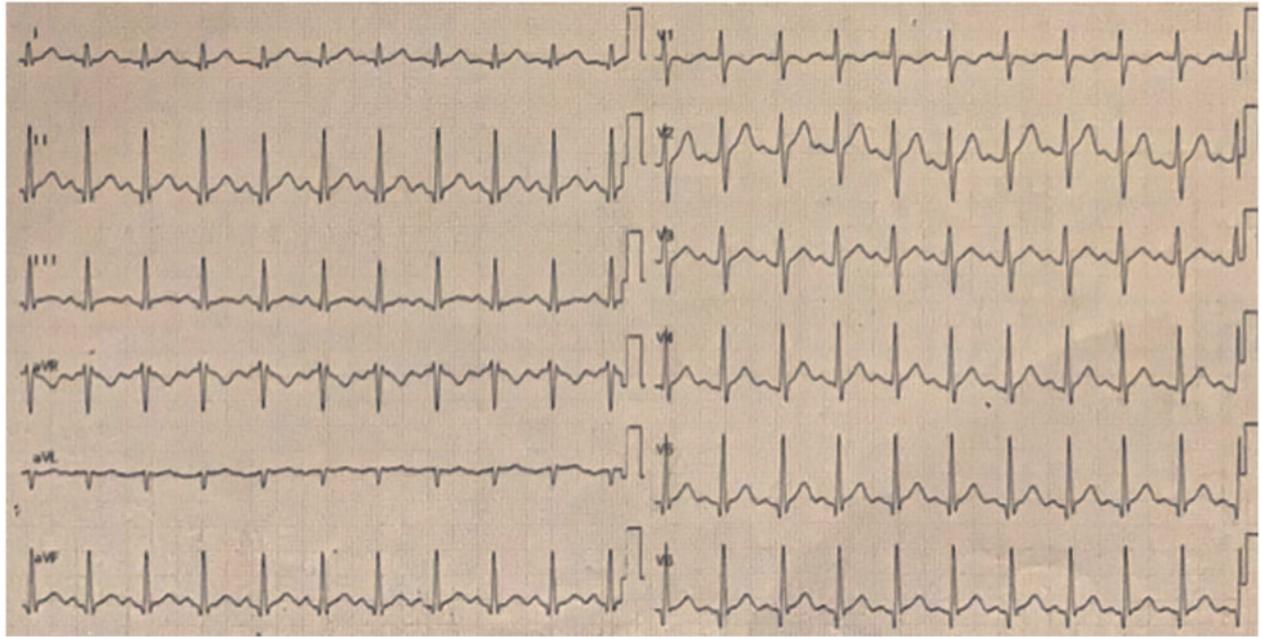


Figure 1 Electrocardiogram showing tachycardia at 128 b.p.m. and diffuse, non-specific, concave ('saddle-shaped') ST-segment elevations in all leads except aVR and V1 and PR-segment depression except in aVR.

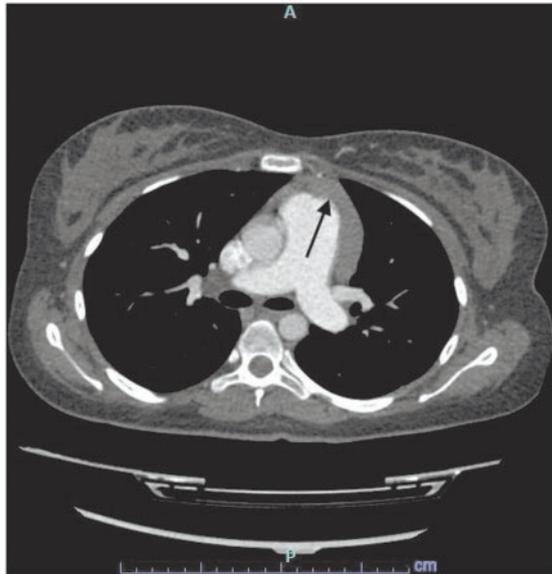


Figure 2 Non-electrocardiogram-gated chest computed tomography with contrast agent—transverse plane, showing presence of a pericardial effusion with slightly increased density (with radiological characteristic not consistent with blood nature) having a maximum thickness of 15 mm in the upper mediastinum.



Figure 3 Cardiac RM—TIRM sequences (turbo inversion recovery magnitude), T2—short-axis view, showing a mass of 73 × 51 mm located in the upper mediastinum.



Figure 4 The same RM scan in orthogonal view, showing minimal pericardial effusion near the anterior mid-basal wall of the left ventricle where the mass has contact with the pericardium in absence of infiltration of the pericardium itself.

significant abnormalities: serum Beta 2 microglobulin, electrolytes, lactate dehydrogenase, and transaminases (ALT, AST) were normal and renal function was not impaired, thus ruling out uraemic pericarditis. Thyroid-stimulating hormone (TSH) was suppressed (<0.0008 mIU/L, local lab normal reference range: 0.4–4 mIU/L) and serum-free thyroxine 4 was increased (61.24 pg/mL, reference range: 8–19 pg/mL); cardiac markers and acute-phase proteins were still negative. Antithyroid therapy was optimized, increasing methimazole dosage to 10 mg TID, and oral propranolol 10 mg TID was introduced. Laboratory tests for autoimmune diseases were performed and the antinuclear antibody panel, lupus anti-coagulant, and anti-neutrophil cytoplasm antibodies were negative. Additionally, anti-mitochondrial (AMA, M2), anti-extractable nuclear antigens, anti-actin smooth muscle antibodies, and anti-Scl-70 (topoisomerase I) antibodies were negative, excluding systemic autoimmune and auto-inflammatory causes of pericardial diseases such as systemic lupus erythematosus, scleroderma and vasculitis. Tests for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (nasopharyngeal swab), Epstein-Barr virus, human immunodeficiency virus, hepatitis C virus, Enterovirus, Parvovirus B19, and Adenovirus were also negative, so that the main viral infectious causes of pericarditis were excluded. Transthoracic echocardiography showed normal left ventricular ejection fraction (EF = 65%), absence of valvular diseases, no pericardial effusion, and normal right ventricular dimensions and function. Thoracic non-ECG-gated CT angiography was then performed (Figure 2) and acute aortic and pulmonary diseases were ruled out. The CT showed the presence of a pericardial effusion with slightly

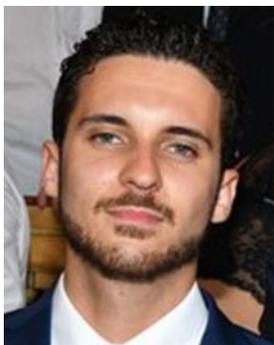
increased density (with radiological characteristic not consistent with blood nature) having a maximum thickness of 15 mm in the upper mediastinum. To characterize this effusion, gadolinium cardiac magnetic resonance imaging (MRI) was performed and the effusion turned out to be an extrapericardial mass of 73×51 mm (Figures 3 and 4) located in the upper mediastinum. A minimal pericardial effusion was found near the anterior mid-basal wall of the left ventricle where the mass had contact with the pericardium. The pericardium, however, showed no signs of infiltration by the mass and no late gadolinium enhancement was described. In view of this and in the absence of surrounding lymphadenopathies, the haematology specialist indicated biopsy of the mass, which was then performed through video-assisted thoracoscopic surgery. Histological analysis showed true thymic hyperplasia and, from an anatomopathological point of view, prevalence of thymic cortex with various Hassall's bodies in the absence of lymphoid infiltration was described. After the improvement of the symptoms, the patient was discharged and ambulatory follow-up was planned. At the 1-month follow-up visit on 4 November 2020, the patient was asymptomatic, TSH levels were normal (3 mIU/L), anti-TSH receptor antibodies (TRAb) were 10 IU/L (vs. 35.50 IU/L on admission; reference range <0.55 IU/L), and a 12-month cardiac MRI was planned.

Discussion and conclusion

To the best of our knowledge, this is a very rare case of thymic hyperplasia presenting as acute pericarditis in which cardiac MRI played a crucial role in the diagnostic and therapeutic approach. The association between mediastinal masses and pericardial symptoms has already been described, and the chest CT has always been a useful first level examination. Thymic hyperplasia is a rare condition of benignity of thymic tissue without mitosis, necrosis, or atypical cells. It is known that this condition can be associated with Graves' disease.⁴ The exact mechanisms through which thyroid hormones exert influence on thymic growth remain unclear. It is known that thymic epithelial cells produce hormone-like substances that are required for T-lymphocyte differentiation and function.⁵ In one study, it was documented that patients with Graves' disease have, on average, higher thymic volumes than controls.⁶ It has also been documented that in some cases antithyroid therapy could induce a regression of thymic volumes.⁷ Acute pericarditis can be an uncommon symptom of this disease, although it is not clear whether this is due to hyperthyroidism itself, or to direct effect of hyperplastic tissue causing local irritation and inflammation due to friction with the moving pericardium. The chest CT is usually sufficient for detecting thymic enlargement, but sometimes a second level examination is needed.^{4,8,9} This case highlights the importance of cardiac MR imaging in the appropriate clinical context, such as that of Graves' disease and with symptoms of acute pericarditis. This investigation provided accurate characterization of the mediastinal mass, despite the inconclusive findings on the chest CT. Although the role of cardiovascular magnetic resonance (CMR) imaging is widely recognized in the differential diagnosis of mediastinal masses, this is the first case of acute pericarditis and thymic hyperplasia in a patient

diagnosed with Graves' disease in which CMR provided a substantial contribution.

Lead author biography



Mauro Acquaro is a second-year cardiology resident at University of Pavia in the IRCCS San Matteo Hospital. He graduated in Medicine in 2018 and had a post-graduation experience as an Emergency Physician at ASST Pavia—Voghera Hospital (Pavia). His areas of interest are mainly clinical cardiology, imaging, pathophysiology of heart failure and research.

Supplementary material

[Supplementary material](#) is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

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References

1. Adler Y, Charron P, Imazio M, Badano L, Barón-Esquivias G, Bogaert J et al.; ESC Scientific Document Group. 2015 ESC Guidelines for the diagnosis and management of pericardial diseases. *Eur Heart J* 2015;**36**:2921–2964.
2. Ghosh AK, Crake T, Manisty C, Westwood M. Pericardial disease in cancer patients. *Curr Treat Options Cardiovasc Med* 2018;**20**:60.
3. Airel PS, Steele MB, Lin AH, Seidensticker DF, Shwayhat AF. Pericarditis, thymic hyperplasia, and Graves' thyrotoxicosis: case report and review of the literature. *Mil Med* 2013;**178**:865–869.
4. Haider U, Richards P, Gianoukakis AG. Thymic hyperplasia associated with Graves' disease: pathophysiology and proposed management algorithm. *Thyroid* 2017;**27**:994–1000.
5. Fabris N, Mocchegiani E, Mariotti S, Pacini F, Pinchera A. Thyroid function modulates thymic endocrine activity. *J Clin Endocrinol Metab* 1986;**62**:474–478.
6. Murakami M, Hosoi Y, Negishi T, Kamiya Y, Miyashita K, Yamada M et al. Thymic hyperplasia in patients with Graves' disease: Identification of thyrotropin receptors in human thymus. *J Clin Invest* 1996;**98**:2228–2234.
7. Budavari AI, Whitaker MD, Helmers RA. Thymic hyperplasia presenting as anterior mediastinal mass in 2 patients with Graves' disease. *Mayo Clin Proc* 2002;**77**:495–499.
8. Baron RL, Lee JK, Sagel SS, Levitt RG. Computed tomography of the abnormal thymus. *Radiology* 1982;**142**:127–134.
9. Baron RL, Lee JK, Sagel SS, Peterson RR. Computed tomography of the normal thymus. *Radiology* 1982;**142**:121–125.